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E) Funding Status

- 1) Granting Agency: Biotechnology Resources Program, DRR, NIH.
- 2) Grant number: RR-643.
- 3) Period of award: This is the 3rd year of the second 3-year period of the Resource.
- 4) Direct cost funds for the period September 1, 1976 to August 31, 1977: \$336,314.
- 5) A proposal for a five-year extension of the Rutgers Resource was submitted in October 1976. The proposal is currently being evaluated by NIH. In our proposal we are requesting a substantially higher level of funding in order to cover increased levels of effort in all areas of the Rutgers Resource, and also to support the acquisition/enhancement of the RUTGERS-10 computer which we propose to use, in coordination with the SUMEX-AIM facility, as a shared resource for the national AIM community.

II) INTERACTIONS WITH THE SUMEX-AIM RESOURCE

During the past year we have continued to use the SUMEX-AIM resource for program development and testing, for communications between collaborators distributed in different parts of the country and for preparation and running of the AIM Workshop. We continue to access SUMEX-AIM via TYMNET, and to a smaller extent via ARPANET. SUMEX-AIM played a key role in consolidating our network of collaborators in ophthalmology (ONET) and in providing the support needed for establishing a productive collaboration among the ONET investigators. Also, it has been most useful in communicating, planning and helping to set up the information pool for the Second AIM Workshop.

Computing in the Rutgers Research Resource continues to be distributed between SUMEX-AIM and the RUTGERS-10. The two computers are providing complementary resources for our research and for our national collaborations. At present, the distribution of our computing is about 3 to 1 between RUTGERS-10 and

SUMEX-AIM. Our total demand at SUMEX-AIM is estimated at about 5000 connect hours for the current year with most of the work done in INTERLISP (about 80% of our total connect hours) and the rest devoted mainly to communications and to limited program testing within ONET.

The SUMEX-AIM facility was used for demonstrations of AIM programs in first year classes and in second year seminars at the Rutgers Medical School, CMDNJ; CASNET, MYCIN, INTERNIST and PARRY were interactively accessed in these classes and seminars. Another innovative use of SUMEX-AIM has been the collaborative development of the AI HANDBOOK, which is intended to provide a computer-based and network accessible encyclopedic coverage of the AI field for the AIM community and AIM guests. The AI HANDBOOK was initiated by Dr. E. Feigenbaum and his students at Stanford. During the year, a graduate class at Rutgers, given by Dr. S. Amarel, worked on the AI HANDBOOK and contributed several articles.

We find that the SUMEX-AIM bulletin board plays an important role in communicating ideas and information on services among users. Since the MYCIN group at Stanford regularly posts summaries of meetings; and other technical information, on the MYCIN bulletin board, we have been able to keep track of their program and problems. This was particularly useful for our work on IRIS where concepts close to the MYCIN CF formalism are being studied.

System support at SUMEX-AIM has been more than good; it has been friendly. Problems or questions concerning the system are consistently handled quickly and competently by SUMEX-AIM staff. Service is simply outstanding.

The system is under heavy usage for most of the day, which causes painfully slow response times for large jobs; thus, it is usable for Rutgers users in the early morning or in the late evening. In most days the load average stays over 7 from noon EST to about 7 p.m. During these hours, the computer is only marginally useful for work with a large LISP system such as IRIS (currently this system has 245 pages of an INTERLISP core image).

For relatively small jobs (about 70 pages), the response time has improved consequent to the changes in the scheduler in early Spring.

Access to SUMEX-AIM via TYMNET has improved considerably. Occasionally, however, problems persist with spurious characters and with broken connections.

In the last year, several new areas of collaboration between Rutgers and SUMEX-AIM have developed, mostly along the lines of systems and support software. These include the following specific efforts:

1. MAINSAIL. During the past year, the design of the MAINSAIL system has been stabilized to a great degree, and Rutgers has followed the development of the MAINSAIL effort in order to be in a position to apply it to Rutgers' AIM activities, particularly in the ophthalmology area. We have made several passes over the MAINSAIL design during this period, with particular interest to the issues of memory allocation and the possibilities of doing list processing in MAINSAIL.

During April, Clark Wilcox and others from the Stanford group installed a prototype MAINSAIL system on the Rutgers PDP-10, and it is presently being

used by a group from NIH who are interested in evaluating MAINSAIL for their own work.

2. SOFTWARE. Two text processing programs, TVEDIT and PUB, were brought over from SUMEX and installed at Rutgers, and are now being used on the RUTGERS-10. These tools, which were developed at Stanford's IMSSS and AI Laboratories, reduce the overhead in program and document preparation and maintenance.
3. ALLOCATION and ARCHIVING. The design of the allocation and archiving systems that have been in use at SUMEX have been adopted, with some modification, for use at Rutgers. One of the important products of the SUMEX research has been the models for interaction between a variety of collaborators; the way in which the allocation of system file space and the archiving of unneeded files have been accomplished at Stanford have been adopted at Rutgers.
4. CG: A program for Explanation of an AI System. In a somewhat different area, Prof. David Levine of the Rutgers faculty collaborated with Dr. Ray Carhart of the Stanford Heuristic Programming Project to produce a program that provides a dynamic, display-oriented interface to the CONGEN program. CONGEN examines the chemical formulas that are possible from a particular empirical formula, under a set of constraints on the generation of formulas. CG, the program that effects this interface, was written at Rutgers, and can run either at Rutgers or at SUMEX-AIM; CONGEN, which is currently written in INTERLISP, runs only at SUMEX-AIM.
5. SYSTEM MODEL: The SUMEX staff has continued to be a model of cooperation and support for research. More importantly, the protocols that the SUMEX staff have developed for solving problems of system/user and user/user interaction continue to be models that we find it possible to apply to the Rutgers environment.

III. FUTURE PLANS OF THE RUTGERS RESOURCE; RELATIONS TO SUMEX-AIM

Our plans for the future are to continue along the main lines of our current research. We expect our computing needs to grow at a rate of about 20% per year. About a quarter of our total computing will be done at SUMEX-AIM; most of this work will be concerned with large program development (mainly in INTERLISP).

In our application for renewal of the Resource grant (which is currently being reviewed at NIH) we propose to acquire and augment the RUTGERS-10 computer in order to provide sufficient capacity to satisfy the projected computing demand of the Rutgers Resource, and also to provide added computing capacity for the national AIM community and to enlarge the scope of the AIM resource sharing activities. We are proposing a KL-10 configuration with TOPS-20 software, which promises compatible operation with the TENEX system at SUMEX-AIM. We expect the configuration to have 50% more capacity than the present RUTGERS-10 in the first year of the renewal period. Two thirds of the enhanced system capacity will be allocated to the Resource; this capacity share will be evenly divided between internal Resource projects and the national AIM community. We expect the

RUTGERS-10 to be operated in close coordination with the SUMEX-AIM facility, within a common management framework. This plan will provide an additional node to the AIM network. We envision a move towards specialization and differentiation of functions among the nodes in the network. We propose to use the Rutgers AIM center for promotion of AI applications in clinical medicine (and in related biological modeling) with special emphasis on collaborative network-based projects of the type that have developed within our Resource to date.

In addition to our computing plans, we propose to increase our AIM dissemination and training efforts (AIM Workshops, conferences, post doctoral programs), and to continue our system development activities with the aim of enhancing scientific communications within the AIM community and between AIM researchers and other interested scientists. We expect increased collaboration with SUMEX-AIM in these areas.

6.3 PILOT STANFORD PROJECTS

The following are descriptions of the informal pilot projects currently using the Stanford portion of the SUMEX-AIM resource pending funding, and full review and authorization.

6.3.1 GENETICS APPLICATIONS PROJECT

Computer Science Applications in Genetics

Prof. L. L. Cavalli-Sforza
Department of Genetics
Stanford University School of Medicine

We have been quite satisfied with the use of programs such as REDUCE, MLAB, SPSS. REDUCE has been used by graduate student D. Wagener, to check algebra, and also by L. Cavalli-Sforza and has been of great help in circumstances in which algebraic manipulations were too lengthy for hand verification. Unfortunately REDUCE has a maximum length of algebraic expansions that can be manipulated by computer, which is not always generous enough for our purposes; the maximum allowed was increased but there is now no warning as of when the length of expression overruns the new limits. The penalty is the total loss of the information. If this could be mended, the program would be much more useful. MLAB is very useful for least square fitting of complex systems of equations. SPSS is widely used and well known; it is working fine in the system.

Special modelling efforts involved: 1) a program of information storage and retrieval which may be useful also for analysis of multi-dimensional contingency tables. The material to which it was applied derives from anthropological and archeological survey and excavation data in Calabria, Italy by A. Ammerman. The information collected on coordinates of sites, material found, elevation, land form, soil, ecological and geological data etc. refers to hundreds of sites and will eventually be subject to analysis according to models of growth and spread of Neolithic populations. It is eventually hoped to investigate the power of new techniques of statistical analysis, employing spectral analysis of the matrices representing the data. 2) Similar situations, on the basis of other data available from the literature, are also being investigated by means of simulations of the population growth and spread, e.g. for the Bandkeramik populations in Central Europe. It is thus hoped to obtain, eventually, an explanation of the geographic distribution of genes in Europe, the Middle East and nearby areas, based on the hypothesis that the present distribution reflects predominantly a major radiation of a population of farmers which took place with the spread of agriculture from the Middle East, from 9000 to 5000 years ago. 3) The geographic distribution of genes, as observed today, is analyzed by means of gene frequency maps. We have developed many methods of interpolation of data for map construction, and many methods of graphical display of the maps obtained. We are currently comparing the methods of construction of maps. Some of the methods of construction are fairly sophisticated, but more work will be necessary to develop further our programs so that they can be considered to interpolate intelligently. Our tests of validity are based on eliminating each observation in turn, computing its expected value with the observed one (a sort of jack-knifing). It is clear that results could be improved if this procedure could be carried out simultaneously for several genes and alleles; at the moment it is done for one allele at a time. The simultaneous analysis is an ambitious program but would considerably improve present results. At the moment, for instance, we have no way to make gene frequencies of all alleles at a locus sum to 100% (except approximately, because we cannot consider more than one allele at a

time). In addition, other information on the populations (whether they are isolates, etc.) could be introduced, and verified by the program. Also, specific hypotheses on the evolutionary factors affecting the gene frequencies could be tested more directly. At the moment, the major limitation to these more sophisticated analyses is the availability of computer space.

6.3.2 BAYLOR-METHODIST CEREBROVASCULAR PROJECT

Baylor-Methodist Cerebrovascular Project

John L. Gedye, M.D.
Data Services Research Laboratory
Department of Neurology, Baylor College of Medicine

During the year the Data Services Research Laboratory has had a total of about 2,500 hours of man-effort available, of which about 5% has been devoted to activities directly related to the Sumex pilot study.

I) Summary of research program

A) Technical goals

The general goal of the laboratory - the creation of a computer-based system for the support of clinical research in neurology, as described in the 1975-76 annual report - remains unchanged.

In spite of the limited manpower available during the year, good progress has been made toward the specific goal of developing the PDP11/35-based clinical research system 'CLINSYS' to a point where it can begin to give real support to Departmental projects.

We have made good progress in recent weeks with the development of software which will allow easier access to the resources of SUMEX for users of our local system. It is now possible to give the command 'SUMEX' to our local system executive and have the entire login procedure through to receipt of the "final" SUMEX 'Q' carried out automatically. Control characters allow the user's terminal to be switched between SUMEX and the local system, and these have been chosen to be compatible with the BANANARD control characters, so that this can be operated without interference.

Facilities have been provided which allow ASCII files to be created on either system and transferred to the other. These facilities will operate under our local PDP11/35 batch system, and we have tested them by creating a test data file of about 1,000 ASCII characters on an account on the PDP11/35, and submitting a batch job (to run at specified time) which logs into SUMEX, transfers the test data file and copies it back again onto the PDP11/35 account and logs out. It then logs in again and repeats the whole process with the latest copy of the file. In this way we hope to estimate the reliability of this form of data transmission - at present it looks as if the error rate will be less than 1 in 16,000 characters - and to lay the foundations for a system that will allow us to make maximum use of SUMEX off-peak time in the projects described below.

B) Medical relevance and collaboration

The development of CLINSYS has continued on the general lines described in the 1975-76 annual report. Specific data acquisition procedures have been designed and implemented for: clinical psychology - both conventional and automated testing techniques have been accommodated; clinical physiology - facilities for the manual entry of Xe133 inhalation regional cerebral blood flow measurements have been provided, and work is now in progress on a system for direct transmission of data to the PDP11/35 from the integral PDP11/05 which is part of the equipment ; and hematology - provision has been made for the acquisition of data from tests of platelet function.

Because of its central importance, a major emphasis has been placed on making provision for the acquisition of suitably summarised CT scan data, and a number of exploratory studies have been carried out with the result that we hope to have the first edition of a 'CT scan system' working in the near future. This will have an important part to play in future projects.

No further progress has been made with the implementation of a work station incorporating the hand-held OCR wand developed by Recognition Equipment Incorporated - which was described in the 1975-76 report - but we intend to make use of such a 'wand' work station in the context of a system for acquiring data from the radiologist's 'CT scan report' as part of the 'CT' record.

C) Progress summary

The aim of our 'pilot study' remains unchanged - to formulate a project relevant to the activities of the Department which will provide an acceptable and legitimate 'point of entry' for artificial intelligence research, and which will allow the systematic formulation of objectives for the future.

Work has continued along the lines discussed in the 1975-76 report, using, as test data, results from 69 demented patients and 15 controls who had had regional cerebral blood flow measurements. This work has led to a promising 'AI' approach which is now being applied to CT scan data, and when the feasibility of this has been demonstrated the way will be open for work to go head on the implementation of a general purpose program.

D) Publications

There are as yet no publications dealing with the 'pilot study' as such. Certain aspects of the work referred to in this report have been mentioned in publications but these are all currently 'in press'. Details are available on request.

E) Funding status

1) Current funding

The work is currently supported by a section of the 3-year grant for the Center for Cerebrovascular Research, but at the present time this is only approved up to January 31st, 1977.

2) Pending applications and renewals

Work is currently in progress on a grant application for submission by July 1st for support for the laboratory from April 1st, 1978. This will concentrate on the use of CLINSYS to support of the study of brain-behavior relations in demented patients using CT scan data and the results of automated behavioural assessment.

II) Interactions with the SUMEX-AIM resource

- A) Little has so far been achieved by way of collaborations through the network, although the SNDMSG facility has been useful for keeping in touch with contacts made at the 1975 workshop.

It is hoped though, that in the future we may be able to test out the concept of a CT scan archive created by the joint efforts of a dispersed community of users.

- B) For some reason I did not hear about the 1976 workshop until it was over, and so far have heard nothing about a 1977 one. I found the 1975 workshop very useful, and would strongly support the continuation of the workshops in some form - particularly if one could get down to fundamentals with people working on similar problems.

I have kept in close contact with Paul Blackwell at Columbia, Missouri since the 1975 workshop, and we last met at an N.S.F. Conference on 'MATHEMATICAL STRUCTURE IN THE HUMAN SCIENCES' at Penn State in March.

- C) I have no criticisms of resource services beyond the usual one of slowness of response time at peak periods.

III Follow on SUMEX grant (8/78 -7/83)

- A) The main long range user goal of relevance is the establishment of a demonstration CT scan reference archive using the resources of SUMEX. It is not clear just what resources this will need, but at the present time it looks as if the feasibility of the approach could be established with an allocation of 500 pages of storage, and possibly less.

- B) The main justification for continued use of SUMEX is that it provides a unique opportunity to explore the possibility of setting up a dispersed CT scan research community with a reasonably high chance of being able to

demonstrate something of potential clinical value in the relatively short term.

- C) I would like to see attention given to the communications potential of the SUMEX resource. We have not been able to make full use of this in last two years because of a lack of local resources, but now that we have our local system interfaced we are beginning to get a real feel for the potentialities. We have also found that visitors to our laboratory are very impressed with the ease of setting up the interface, and many - including computer company representatives - have confessed to being unaware of the possibilities provided by the existing technology. In particular we have found little experience of the use of autodiallers.

6.3.3 COMPUTER ANALYSIS OF CORONARY ARTERIOGRAMS

Computer Analysis of Coronary Arteriograms

Donald C. Harrison, M.D., Edwin L. Alderman, M.D., and Lynn Quam, Ph.D.
Division of Cardiology, Stanford University Medical School

The goal of this project is to develop computer techniques for automatic acquisition of the anatomic distribution of coronary arteries and a quantitation of the degree of narrowing of these vessels. In order to do this, two different types of image processing techniques will be developed. First, a three-dimensional representation of the coronary arterial tree will be automatically constructed from coronary arteriograms taken sequentially from several different views. Second, the amount of stenosis will be measured by combining information from multiple sequential frames in order to improve resolution and reduce radiographic noise.

BACKGROUND:

Coronary arteriography is the definitive test for the evaluation of patients with coronary artery disease. There is no other test currently available which provides information concerning the location and severity of coronary narrowings and the distribution of coronary blood vessels in the myocardium. Numerous studies document that prognosis in patients with coronary disease reflects the severity of anatomic disease. Coronary vascular anatomy and the extent of lesions are, in an epidemiologic sense, more precise indicators of prognosis than are clinical symptoms.

At the present time, categorization of the extent of coronary vascular disease is based somewhat simplistically on the number of major coronary vessels involved and a rough estimate of the percentage obstruction. Computer representation of the coronary tree, coupled with either interactive or automatic entry of degree of stenosis will permit the development of more precise indices of anatomic disease of the myocardium.

Computer image processing techniques offer the possibility of objectively measuring the severity of coronary stenosis, both at the point of maximal narrowing and averaged over a segment of the vessel.

APPROACH:

An extensive set of image processing functions have been developed and applied to detect the regions of the arteriograms which correspond to the arterial tree. These regions are then transformed to a "skeleton" which roughly corresponds to the midlines of the vessels in the arterial tree. This skeleton is then transformed to a graph representation which can be topologically and geometrically analyzed to distinguish vessel intersections (in the 2-d projection, not real 3-space intersections) from vessel bifurcations. The result is a graph structure interpretation of the arterial tree with quantitation of the

locations (2-d) of bifurcations, and for each vessel segment the path of the vessel midline and the vessel diameter. The computer algorithms are described in more detail in the following sections.

Data Acquisition:

We have digitized a number of 35 mm cine frames from three subjects using both an Optronics film scanner and a Dicomed film digitizer operating at 25 and 50 micron pixel resolution. For each subject frames are manually selected to provide good contrast in the proximal vessels from both LAO and RAO projections and be approximately synchronized within the cardiac cycle.

Pre-processing:

The digitized frames are computer enhanced using high frequency filtering to eliminate the x-ray exposure gradient and emphasize sharp edges which tend to correspond to the vessels.

High contrast areas in the enhanced frames are detected by a simple threshold region detector. Currently, many regions are detected which do not correspond to the arterial tree, but are caused by background features such as vertebra. We are in the process of digitizing another set of frames which have been chosen to include time synchronized pre-injection frames in order to permit background subtraction. The result of this step is a binary image corresponding to high density areas in the frame.

The root of the arterial tree is manually specified by the operator, and a connected point region grower finds all points connected to the root. This usually finds all medium and large sized vessels, and some smaller vessels. Unconnected background is totally eliminated. Sometimes, substantial pieces of the arterial tree are not connected to the root. When this occurs, the operator can run the region grower from new starting points. The result of this step is a binary image corresponding to most of the arterial tree.

We expect that by using background subtraction we can very reliably detect the arterial tree and eliminate most of the manual "hand-holding" in the previous steps.

Arterial Tree Graph Formation:

The binary image of the arterial tree is "skeletonized" by computing the distance transform of the image and connecting peaks and ridges in distance. The distance transform computes for each point in the image, the Euclidean distance to the nearest zero (point not in region). Points at vessel midlines are easily detected because they are local maxima (ridges) in distance from their vessel walls.

The 2-dimensional array of ridge-peak information is next processed to form a graph structure describing the connectivity of vessel segments (distance ridges) to nodes (points where 3 or more ridges converge).

The graph is simplified by detecting and eliminating insignificant terminal segments which are usually the result of noise in the image.

We have now accomplished a significant simplification of the data from the original 2-dimensional array of x-ray density data to an essentially 1-dimensional description of the vessel midlines and points of bifurcation and intersection. This data (when vessel width is included) is sufficient to completely reconstruct the binary image of the arterial tree.

Topologic and Geometric Graph Analysis:

The graph is next analyzed to determine the proximal-distal orientation of each vessel segment. Starting at the distal node of a vessel segment, all segments which are attached to that node must be within 90 degrees in pointing direction. Any segment violating this rule is identified as an intersection. Starting from the root of the arterial tree, all segments are classified by this procedure.

Nodes which have been identified as intersections are now analyzed in order to correspond distal segments with proximal segments according to the a set of rules about arterial topology and geometry.

Having resolved vessel intersections, we now transform the graph to a simple tree structure which corresponds topologically to the arterial tree.

Future Directions:

The above computer algorithms have been successfully applied to the images in a few sets of digitized data. We plan to digitize frames prior to injection to enable background subtraction, which we believe will greatly improve the reliability and accuracy of the initial vessel detection. The algorithms have not yet been tried on cases with abnormal angiograms, and we expect that as more cases are incorporated into our image library, it will be necessary to develop more rules and analytical techniques in order to properly interpret the 2-dimensional images.

Based on the encouraging progress which has been made in processing coronary arteriograms and based on other areas of expertise in image processing within the Stanford University Medical Center, we have developed and submitted on November 1, 1976 to the NHLBI a new grant proposal titled "Computerized Medical Image Processing Laboratory". This proposal contains a detailed report of the progress had been made up to that time and details the further steps which we propose to pursue.

USE OF SUMEX RESOURCE:

Work of this project has been dependent on the SUMEX facility for several reasons. First, this project has not been funded to provide its own computer facilities. Second, although the Stanford Division of Cardiology does have minicomputer systems which could be used for this project, it is considerably

easier to develop image processing and artificial intelligence techniques on a larger scale system in which many powerful tools already exist. It is important in the research phase of this project to be able to easily and quickly perform experiments, without the difficulties of fitting the experimental programs into the small computer memory environment.

We believe that our use of the SUMEX facility is completely within the guidelines for SUMEX use, since our primary purpose is to develop image analysis and understanding techniques for the quantitation of coronary artery disease. A secondary result of this research project is the development of general purpose image analysis and modelling algorithms.

SPONSORSHIP:

Granting agency: NIH
Grant : 5 RO 1 HL18870-02
Period of award: 06/01/76 - 05/31/78
Current annual funding: \$20,807 + indirect costs

6.3.4 QUANTUM CHEMICAL INVESTIGATIONS

Theoretical Investigations of Heme Proteins and Opiate Narcotics

Dr. Gilda Loew
Department of Genetics
Stanford University

(Grant, PCM 76 07324, 2 years, \$20,500 this year)

SUMEX is used for the calculation of various one-electron electronic properties of iron containing compounds. The programs were formulated and written by David Steinberg, Michael Chadwick and David Lo. David Lo was responsible for converting the program for interactive use on the PDP system. Slight improvements were made by Robert Kirchner and Sheldon Aronowitz has expanded the formulation to include additional spin and oxidation states of the iron atom.

The properties that are calculated include the electric field gradient at the iron nucleus, quadrupole splitting, isotropic and anisotropic hyperfine interaction, spin-orbit coupling and zero field splitting, g values and temperature dependent effective magnetic moments. The calculated values are compared directly to experimental results obtained from published Mossbauer resonance and electron spin resonance spectra. Such a comparison determines not only the reliability with which these properties can be calculated but also gives an indication of the ability of the model of the iron active site to mimic the actual environment found in a particular compound or iron containing protein.

The major input to these properties programs is a description of the electron distribution of the compound under consideration. This description is obtained using a semi-empirical molecular orbital method employing the iterative extended Huckel procedure. Such a calculation requires up to 660K core and is performed elsewhere. When the calculated electron distribution yields a set of calculated properties in agreement with observation, we have increased faith in the description of the model of the active site and can carry the model one step further to make qualitative inferences about certain properties relevant to the biological functioning of the compound.

We are currently performing a systematic study of heme proteins. The electromagnetic properties of these proteins and of synthesized model compounds which mimic the observed behavior of the proteins have been well studied experimentally. Specifically, we have addressed the following problems:

- (1) Cooperativity of oxygen binding to hemoglobin. Calculations have been made for high and low affinity forms of deoxyhemoglobin. This work has been submitted to Nature (Loew and Kirchner).
- (2) The nature of oxygen binding to the heme unit. Calculations were made of model oxyheme compounds with varying oxygen geometry and electron configuration. This work is now in press in the Journal of the American Chemical Society. (Kirchner and Loew).

- (3) The enzymatic cycle of an oxidative metabolizing heme enzyme called cytochrome P-450. This enzyme is responsible for drug metabolism and toxicity and for activation of many chemical carcinogens. Preliminary characterization of the enzymatically active state has been made. This work is in press in the Journal of the American Chemical Society (Loew, Kert Hjelmeland and Kirchner).

In a completely different context, we have been using SUMEX to calculate the conformation of pentapeptides (enkephalins) which have been recently found to be endogenous opiates. The aim of this study is to determine in what way, if any, they can mimic the structure of prototype opiates such as morphine and meperidine. For this work, we use a protein conformation program with empirical interaction potentials. Quantum mechanical conformations calculations of the same peptides are being performed by us elsewhere and the results of the two methods being compared.

6.4 PILOT AIM PROJECTS

The following are descriptions of the informal pilot projects currently using the AIM portion of the SUMEX-AIM resource pending funding, and full review and authorization.

6.4.1 COMMUNICATION ENHANCEMENT PROJECT

Communication Enhancement Project

John B. Eulenberg, Ph.D. and Carl V. Page, Ph.D.
Department of Computer Science
Michigan State University

I) Summary of research program.

A) Technical goals.

The major goal of this research is the design of intelligent speech prostheses for persons who experience severe communication handicaps. Essential subgoals are:

- (1) Design of input devices for persons with greatly restricted movement.
- (2) Development of software for text-to-speech translation.
- (3) Research in knowledge representations for syntax and semantics of spoken English in restricted real world domains.
- (4) Development of micro-computer based portable speech prostheses.

B) Medical Relevance and Collaboration.

We have exchanged visits and had many conversations with Dr. Kenneth Colby of UCLA who is working on similar problems for a domain of people who have aphasia.

The need for such technology in the medical area is very great. Millions of people around the world lead isolated existences unable to communicate because of stroke, traumatic brain injury, cerebral palsy, and other causes. The emergence of inexpensive micro-processors and sound synthesizers makes it possible to develop devices now that can be the prototypes for widespread use.

We have organized institutes to bring together the many professionals who have an interest in this area. Together with the Tufts New England Medical Center, the TRACE Center of the U. of Wisconsin, and the Children's Hospital at Stanford, we have begun the first newsletter for dissemination in this area. Dr. John B. Eulenberg helped to organize the first Federal workshop for governmental agencies who have some interest in funding work in these areas. Represented were the Bureau of Education for the Handicapped, The Veterans Administration, NIMH, NINCDS, NSF, and others. We have also been in touch with United Cerebral Palsy associations at the state and national levels. There is much interest in this area from medical, educational, and governmental communities, but no traditional means of supporting it.

C) Progress summary.

Although some facets of the research have been underway at MSU for several years, we have been using SUMEX-AIM for only six weeks at this time, having received our password in March, 1977. During the last six weeks, we have:

- 1) Designed and built hardware and software allowing us to transmit files to SUMEX from our Nova 2/10 at 300 baud.
- 2) Organized a research team of 4 students possessing background in artificial intelligence led by Dr. Carl V. Page to develop a semantics-based speech generator. We expect to have a prototype running in June (written in SAIL). To this end we are concentrating on semantics associated with personal needs, small talk (weather etc.), and perhaps obtaining geographic directions.
- 3) Have begun conversion of ORTHOPHONE, MSU's large English text-to-speech program from its CDC6500 Fortran implementation to a SAIL version. 4) Obtained temporary local support for terminals and tie-lines to use the SUMEX-AIM facility. We requested these in our original proposal but were not granted them. We have to share with others in the use our tie-lines and terminals. At present the lack of a dedicated tie-line from East Lansing to Tymshare in Ann Arbor or Detroit is a problem for us during 0600 to 0900 PST.

During the past few months, Dr. Richard Reid of our project has:

- 5) Developed a personal communication system for a 10-year-old person who has cerebral palsy. It is micro-computer-based and can accept inputs via an adaptive switch from a series of menus displayed on a TV screen, via Morse code, or by a keyboard. Its outputs can be TV display, hard copy, Morse code, spoken English, Morse code, or musical sounds. We expect to use knowledge gained from the SUMEX-AIM semantics project to specify the content and connection of the choice menus for this project.

During the past three months,

- 6) We have begun to experiment with the interaction of knowledge sources (letter and word frequencies, syntactics, semantics and pragmatics) as a means of anticipating likely inputs and displaying them for a person to choose from.
- 7) Built and tested a myoelectric interface and used it (together with a miniature FM transmitter) for input of changing muscle potentials into a computer. There is reason to believe that this means of input may provide a higher bit rate than any other known means for those people who experience severe motoric problems due to cerebral palsy.

D) Up-to date list of publications. (1976 to date)

For John B. Eulenberg:

- "Technical Systems Development, Headend", Interim Report, April, 1976, Experimental Applications of Two-Way Cable Delivery, NSF Grant No. APR 75-14286.
- "Interactive New Hired Information Access System with Both Voice and Hard Copy Output: User's Guide to NHQUERRY", April 11, 1976 (With Steven Kludt and Jerome Jackson (Artificial Language Laboratory Report AEB 041176))
- "Language Individualization in a Computer-Based Speech Prosthesis System", National Computer Conference, New York, June 9, 1976.
- "Individualization in a Speech Prosthesis System", Proceedings of 1976 Conference on Systems and Devices for the Disabled, June 10, 1976.
- "The LEAF Language", Interim Report, September, 1976, NSF Grant No. APR 75-14286.
- "A Programmable Multi-Channel Modem Output Switch", September 22, 1976, with Joseph C. Gehman and Juha Koljonen (Artificial Language Laboratory Report AEB 092276)
- "SMPTE Time Code Interface and Computer-Controlled Video Switcher", with Michael Gorbitt and Dennis Phillips, Interim Report, March, 1977 NSF Grant APR 75-14286.

For Carl V. Page:

- "Heuristics for Signature Table Analysis as a Pattern Recognition Technique", IEEE Transactions on Systems, Man and Cybernetics, Vol. SMC-7, No. 2, February 1977.
- "Discriminant Grammars, an Alternative to Parsing". with Alan Filipski, Proceedings of the IEEE Workshop on Picture Processing, Computer Graphics, and Pattern Recognition, April 22, 1977.
- "Pattern Recognition and Data structures". Chapter in "Data Structures in Computer Graphics and Pattern Recognition" Edited by Allen Klinger, Academic Press, 1977.

During 1976 Dr. Eulenberg presented 15 lectures around the country on his research, was interviewed for TV eight times and was on radio five times.

E) Funding Status.

- 1) Current funding. Wayne County (Detroit) Intermediate School District. \$230,000. (second year) Jackson County Intermediate School District \$21,500 (Second year). Both of these are on a one year at a time basis.

Some of this money is being used to purchase equipment which is the property of WCISD or JCISD for use in demonstration classrooms in the schools. Very little of it can be used to support the research goals which we have communicated to SUMEX-AIM because of other commitments in the grant. However, the special communication devices, students, and other research facilities provides the critical mass which will allow us to do the work that we have proposed.

2) Pending applications and renewals.

State of Michigan Vocational Rehabilitation Services \$30,000.
(application)

United Cerebral Palsy Association of Michigan \$50,000. (application)

United Cerebral Palsy Association (National) \$60,000. (For study of control by myoelectric inputs) (application)

Oakland County Intermediate School District \$200,000. (application)

Genessee County Intermediate School District \$200,000. (Being written)

As one can see from this list of sources, there is a lot of interest in this area from agencies which are not experienced in funding high-technology and research, since a mandatory special education act has become law in Michigan.

II) Interactions with the SUMEX-AIM resource.

Again we point out that we have been a part of this community for only about 6 weeks and we will have more to say next year.

A) Examples of medical collaboration and medical use of programs via SUMEX.

The faculty in the MSU College of Human Medicine who teach medical decision making were shown a demonstration of the SUMEX system, MYCIN and PARRY. We plan to present a demonstration to advanced medical students and faculty at the Medical School in the near future.

A member of our Medical School faculty, Dr. Richard Ropple, an expert on myoelectronics, is a member of of our research group.

The Dean of our College of Human Medicine visited our laboratory in April, 1977 and we expect encouragement and collaboration.

B) Examples of sharing, contacts, and cross-fertilization with other SUMEX-AIM projects.

1. We have met with Dr. Kenneth Colby on many occasions including the SUMEX-AIM workshop in June, 1976. Our work in many ways complements his and we have had several worthwhile interchanges of information. We are